

**Amendments To The Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

Claim 1. (previously presented) A formulation comprising penetrants being capable of penetrating the pores of a barrier, the average diameter of said pores being smaller than the average diameter of said penetrants, wherein said penetrants can transport agents or enable agent penetration through said pores after said penetrants have entered said pores, wherein the formulation further comprises

1) at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100% per 6 months, wherein the antioxidant is selected from the group consisting of between 0.0025 and 0.2 w-% of butylated hydroxyanisol, between 0.0025 and 0.2 w-% of butylated hydroxytoluene, between 0.001 and 2 w-% of tertiary butylhydroquinone, between 0.001 and 2 w-% of propyl gallate, between 0.005 and 5 w-% of tocopherols, between 0.001 and 5 w-% of ascorbic acid esters, between 0.001 and 5 w-% of ascorbic acid, between 0.001 and 5 w-% of sodium bisulphite, between 0.001 and 5 w-% of sodium metabisulphite, between 0.0001 and 2 w-% of thiourea, between 0.01 and 5 w-% of cysteine, between 0.01 and 5 w-% of monothioglycerol, between 0.0005–2 w-% of nordihydroguaiaretic acid, between 0.005 and 5 w-% of glutathione, between 0.001 and 5 w-% of EDTA, and between 0.001 and 5 w-% of citric acid, based on the total weight of the formulation; and

2) at least one microbiocide in an amount that reduces the bacterial count of 1 million germs added per gram of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of *Pseudomonas aeruginosa* or *Staphylococcus aureus*, after a period of 4 days, wherein the microbiocide is selected from the group consisting of up to 10 w-% of ethyl alcohol, up to 10 w-% of propyl alcohol, up to 10 w-% of butyl alcohol, up to 10 w-% of benzyl alcohol, between 0.3 – 0.6 w-% of chlorobutanol, between 0.05–0.2 w-% of parabens, between 0.05–0.2 w-% of methyl paraben, between 0.002–0.02 w-% of propyl paraben, between 0.05 – 0.2 w-% of sorbic acid, between 0.1 – 0.5 w-% of benzoic acid, between 0.1 – 0.3 w-% of phenols, between 0.1 – 0.3 w-

% of triclosan, and between 0.01 – 0.05 w-% of chlorhexidine, based on the total weight of the formulation;

wherein the agent is selected from corticosteroids and the relative content of corticosteroids is above 0.1 weight-%, relative to total dry mass of the formulation.

Claim 2. (previously presented) The formulation according to claim 5, wherein said at least one consistency builder is added in an amount that increases the formulation viscosity to up to 1 Ns/m<sup>2</sup>.

Claim 3. (previously presented) The formulation according to claim 1, wherein said at least one antioxidant is added in an amount that reduces the increase of oxidation index to less than 100% per 12 months.

Claim 4. (cancelled)

Claim 5. (previously presented) The formulation according to claim 1, further comprising at least one consistency builder, in an amount that increases the formulation viscosity above that of the non-thickened corresponding formulation to maximally 5 Ns/m<sup>2</sup> so that spreading over, and retention at, the application area is enabled.

Claim 6. (previously presented) The formulation according to claim 83, wherein the polymer weight fractions are in the range between 0.05% and 10%.

Claims 7-12. (cancelled)

Claim 13. (previously presented) The formulation according to claim 1, wherein the corticosteroid is selected from the group consisting of: alclonetasone dipropionate, amcinonide, beclomethasone dipropionate, betamethasone, betamethasone 17-valerate, betamethasone 17,21-divalate, betamethasone 21-acetate, betamethasone 21-butyrate, betamethasone 21-propionate,

betamethasone 21-valerate, betamethasone benzoate, betamethasone dipropionate, betamethasone valerate, budesonide, clobetasol propionate, clobetasone butyrate, cortexolone, corticosterone, cortisone, cortisone 17-acetate, 21-deoxybetamethasone, 21-deoxybetamethasone 17-propionate, deoxycorticosterone, desonide, desoxymethasone, dexamethasone, diflorasone diacetate, diflucortolone valerate, flucolorolone acetonide, flumethasone pivalate, fluoconolone acetonide, fluocinonide, fluocortin butyl, fluocortolone, 9-alpha-fluorocortisone, 9-alpha-fluorohydrocortisone, 9-alpha-fluoroprednisolone, fluprednidene acetate, flurandrenolone, halcinonide, hydrocortisone, hydrocortisone 17-acetate, hydrocortisone 17-butyrate, hydrocortisone 17-propionate, hydro cortisone 17-valerate, hydrocortisone 21-acetate, hydrocortisone 21-butyrate, hydrocortisone 21-propionate, hydrocortisone 21-valerate, 17-alpha-hydroxyprogesterone, methylprednisolone acetate, mometasone furoate, prednisolone, prednisone, prednisone 17-acetate, prednisone 17-valerate, progesterone, triamcinolone, and trimcinolone acetonide.

Claim 14. (previously presented) The formulation according to claim 1, wherein the penetrants are suspended or dispersed in a polar liquid in the form of fluid droplets surrounded by a membrane-like coating of one or several layers, said coating comprising at least two kinds or forms of amphiphilic substances with a tendency to aggregate,

wherein said at least two substances differ by at least a factor of 10 in solubility in said liquid or wherein said substances when in the form of homo-aggregates, for the more soluble substance, or of hetero-aggregates, for any combination of both said substances, have preferred average diameter smaller than the diameter of the homo-aggregates containing merely the less soluble substance; or

wherein the presence of the more soluble substance lowers the average elastic energy of the membrane-like coating in the vicinity of thermal energy.

Claims 15-20. (cancelled)

Claim 21. (previously presented) The formulation according to claim 14, wherein the average penetrant diameter is between 30 nm and 500 nm.

Claim 22. (previously presented) The formulation according to claim 14, wherein the average diameter of the penetrant is 2 to 25 times bigger than the average diameter of the pores in the barrier.

Claim 23. (previously presented) The formulation according to claim 14, wherein the dry weight of all carrier droplets in a formulation for the use on human or animal skin is 0.01 weight-% (w-%) to 40w-% of total formulation mass.

Claim 24. (previously presented) The formulation according to claim 14, wherein the dry weight of all carrier droplets in a formulation for the use on human or animal mucosa is 0.0001 w-% to 30 w-% of total formulation mass.

Claims 25-34. (cancelled)

Claim 35. (previously presented) The formulation according to claim 1, wherein the content of corticosteroids is between 0.1 w-% and 20 w-%.

Claims 36-38. (cancelled)

Claim 39. (previously presented) The formulation according to claim 35, wherein the relative content of corticosteroids is the case of clobetasol or one of its derivatives is below 15 w-%, relative to total dry mass of the drug-loaded carriers.

Claim 40. (previously presented) The formulation according to claim 35, wherein the content of said corticosteroid is below the saturation maximum, defined as the content of corticosteroid at which the corticosteroid begins to crystallize in or outside the carrier.

Claim 41. (previously presented) The formulation according to claim 1, wherein in order to speed up drug action a permeation enhancer is added.

Claims 42–43. (cancelled)

Claim 44. (previously presented) The formulation according to claim 1, wherein said corticosteroid is added in an amount which enables the formulation to be applied corresponding to an area dose, as expressed by the total dry mass of penetrant applied per unit area, of between  $0.1 \text{ mg cm}^{-2}$  and  $15 \text{ mg cm}^{-2}$ , if said corticosteroid is desired to exert a therapeutic effect in the deep subcutaneous tissue or the remote tissues, including the whole body.

Claim 45. (previously presented) The formulation according to claim 1, wherein said corticosteroid is added in an amount which enables the formulation to be applied with an area dose, as expressed by the total dry mass of penetrant applied per unit area, of between  $1 \text{ } \mu\text{g cm}^{-2}$  and  $250 \text{ } \mu\text{g cm}^{-2}$ , if said corticosteroid is desired to exert a mainly local rather than systemic therapeutic effect.

Claim 46. (previously presented) The formulation according to claim 1, wherein consistency and, if necessary other characteristics of the formulation are appropriately selected to enable spraying, smearing, rolling or sponging of the formulation on the application area in particular by using a sprayer, spender, roller or sponge.

Claims 47–50. (cancelled)

Claim 51. (previously presented) The formulation according to claim 83, wherein the pharmaceutically acceptable hydrophilic polymers are selected from partially etherified cellulose derivatives, comprising carboxymethyl-, hydroxyethyl-, hydroxypropyl-, hydroxypropylmethyl-, or methyl-cellulose.

Claim 52. (canceled)

Claim 53. (canceled)

Claim 54. (previously presented) The formulation according to claim 84, wherein the synthetic phenolic antioxidants are selected from butylated hydroxyanisol (BHA), butylated hydroxytoluene (BHT) and di-tert-butylphenol (LY178002, LY256548, HWA-131, BF-389, CI-986, PD-127443, E-5119, BI-L-239XX), tertiary butylhydroquinone (TBHQ), propyl gallate (PG) and 1-O-hexyl-2,3,5-trimethylhydroquinone (HTHQ).

Claim 55 - 75. (canceled)

Claim 76. (previously presented) The formulation according to claim 85, wherein the parabenes are selected from alkyl-parabenes, including methyl-, ethyl-, propyl-, or butyl-paraben and benzyl paraben.

Claim 77 - 82. (canceled)

Claim 83. (previously presented) The formulation according to claim 5, wherein the consistency builder is selected from the group consisting of:

pharmaceutically acceptable hydrophilic polymers; completely synthetic hydrophilic polymers; natural gums; and mixtures and further derivatives or co-polymers thereof.

Claim 84. (Canceled)

Claim 85. (Canceled)

Claim 86. (previously presented) The formulation according to claim 1, wherein the concentration based on the total weight of the formulation of TBHQ and PG is between 0.005 and 0.2 w-%, of tocopherols is between 0.01 and 0.5 w-%, of ascorbic acid esters is between 0.005 and 0.5 w-%, of ascorbic acid is between 0.005 and 0.5 w-%, of sodium bisulphite or sodium metabisulphite is between 0.005 and 0.5 w-%, of thiourea is between 0.0005 and 0.2 w-%, of cysteine is between 0.05 and 2 w-%, of monothioglycerol is between 0.05 and 2 w-%, of NDGA is between 0.001 and 0.2 w-%, of glutathione is between 0.01 and 0.5 w-%, of EDTA is between 0.005 and 0.5 w-%, of citric acid is between 0.005 and 3 w-%.

Claim 87. (previously presented) The formulation according to claim 1, wherein the concentration based on the total weight of the formulation of BHA or BHT is between 0.005 and 0.02 w-%, of TBHQ and PG is between 0.01 and 0.02 w-%, of tocopherols is between 0.05 and 0.075 w-%, of ascorbic acid esters is between 0.01 and 0.15 w-%, of ascorbic acid is between 0.01 and 0.1 w-%, of sodium bisulphite or sodium metabisulphite is between 0.01 and 0.15 w-%, of thiourea is between 0.001–0.01 w-%, of cysteine is between 0.1 and 1.0 w-%, of monothioglycerol is between 0.1 and 1.0 w-%, of NDGA is between 0.005 and 0.02 w-%, of glutathione is between 0.05 and 0.2 w-%, of EDTA is between 0.01 and 0.2 w-%, of citric acid is between 0.01 and 0.2 w-%.

Claim 88. (previously presented) The formulation according to claim 1, wherein the concentration based on the total weight of the formulation of thiourea is 0.005 w-%, of cysteine is 0.5 w-%, of monothioglycerol is 0.5 w-%, of NDGA is 0.01 w-%, of glutathione is 0.1 w-%, of EDTA is between 0.05 and 0.975 w-%, of citric acid is between 0.3 and 2 wt-%.

Claim 89. (previously presented) The formulation according to claim 1, wherein the bulk concentration based on the total weight of the formulation of ethyl, propyl, butyl or benzyl alcohol is up to 5 w-%.

Claim 90. (previously presented) The formulation according to claim 1, wherein the bulk concentration based on the total weight of the formulation of ethyl, propyl, butyl or benzyl alcohol is in the range between 0.5 – 3 w.-%.

Claim 91. (New) The formulation according to claim 1, wherein the at least one microbiocide is added in an amount that reduces the bacterial count of 1 million germs added per gram of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of *Pseudomonas aeruginosa* or *Staphilococcus aureus*, after a period of 3 days.

Claim 92. (New) The formulation according to claim 83, wherein the completely synthetic hydrophilic polymers are selected from polyacrylates, polymethacrylates, poly(hydroxyethyl)-, poly(hydroxypropyl)-, poly(hydroxypropylmethyl) methacrylate, polyacrylonitrile, methallyl-sulphonate, polyethylenes, polyoxiethylenes, polyethylene glycols, polyethylene glycol-lactide, polyethylene glycol-diacrylate, polyvinylpyrrolidone, polyvinyl alcohols, poly(propylmethacrylamide), poly(propylene fumarate-co-ethylene glycol), poloxamers, polyaspartamide, hydrazine cross-linked hyaluronic acid and silicone.

Claim 93. (New) The formulation according to claim 83, wherein the natural gums are selected from alginates, carrageenan, guar-gum, gelatine, tragacanth, amidated pectin, xanthan, chitosan collagen and agarose.

Claim 94. (New) The formulation according to claim 1, wherein the tocopherols are selected from tocopheryl-acrylate, -laurate, myristate, -palmitate, -oleate, -linoleate, or any other suitable tocopheryl-lipoate and tocopheryl-POE-succinate.

Claim 95. (New) The formulation according to claim 1, wherein the ascorbic acids are selected from 6-o-lauroyl, myristoyl, palmitoyl-, oleoyl, or linoleoyl-L-ascorbic acid.



Claim 96. (New) The formulation according to claim 1, wherein the phenols are selected from cresol, 4-chloro-m-cresol, p-chloro-m-xlenol, dichlorophene, hexachlorophene and povidon-iodine.

Claim 97. (New) The formulation of claim 1, wherein the corticosteroids are selected from glucocorticoids or mineralocorticosteroids.

Claim 98. (New) The formulation according to claim 1, wherein the corticosteroid is propionate.